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Long-Term Outcomes by Clopidogrel Duration and Stent Type in a Diabetic Population With De Novo Coronary Artery Lesions

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Objectives The purpose of this study was to determine whether long-term clinical outcomes differed between bare-metal stents (BMS) and drug-eluting stents (DES) by duration of clopidogrel use among diabetic patients.

Background There is concern that DES are associated with late adverse events such as death and myocardial infarction (MI) secondary to stent thrombosis. However, data on outcomes in diabetic patients remain limited.

Methods We identified 749 patients with diabetes mellitus who underwent stent implantation with either BMS (n = 251) or DES (n = 498) from October 2002 to December 2004. We performed survival analysis on the full cohort and on those event-free from death, MI, or repeat revascularization at 6 months (n = 671).

Results By clopidogrel duration, the event rate for death or MI was 3.2% in the >9-month group, 9.4% in the 6- to 9-month group, and 16.5% in the <6-month group, p < 0.001. For death alone, the event rate was 0.5% in the >9-month group, 4.3% in the 6- to 9-month group, and 10.0% in the <6-month group, p < 0.001. When taking BMS clopidogrel non-users as a referent in the multivariate analysis, the hazard ratio (95% confidence interval [CI]) for death and nonfatal MI for DES clopidogrel users, DES clopidogrel nonusers, and BMS clopidogrel users were: HR 0.22 (95% CI 0.08 to 0.62, p = 0.005), HR 0.39 (95% CI 0.13 to 1.13, p = 0.08), and HR 0.25 (95% CI 0.08 to 0.81, p = 0.02), respectively.

Conclusions Longer duration of clopidogrel use was associated with a lower incidence of death or MI in both the BMS and DES groups. Among clopidogrel nonusers, the incidence of death/MI or death did not differ by stent type. (J Am Coll Cardiol 2008;51:2220–7) © 2008 by the American College of Cardiology Foundation

Diabetes mellitus is present in 25% of patients undergoing percutaneous coronary intervention (PCI) (1). It is a major risk factor for coronary artery disease and a long-recognized predictor of restenosis after balloon angioplasty and stent placement (2,3). Characterized by neointimal hyperplasia, restenosis is more common in the diabetic population and can take a malignant course requiring multiple percutaneous procedures or coronary artery bypass grafting (CABG) (4). Currently, drug-eluting stents (DES) are considered by many as the standard of care for diabetic patients undergoing PCI. Both the pivotal U.S. trials, the SIRIUS (Sirolimus-coated BX Velocity Balloon-Expandable Stent in the Treatment of Patients with De Novo Coronary Artery Lesions) trial and the TAXUS-IV (Polymer-Based Paclitaxel-Eluting Stent in Patients with Coronary Artery Disease) trial, demonstrated efficacy in the diabetic subgroups (5,6). However, concern has been raised that the favorable results among the diabetic subgroups in these trials might not be generalizable (7,8). Several recent reports have shown a greater incidence of late stent thrombosis with DES when compared with bare-metal stents (BMS) (9–12). Multiple predictors of stent thrombosis have been identified, with the strongest predictor being premature discontinuation of clopidogrel (13). Nevertheless, the long-

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term outcomes with DES compared with BMS, adjusted for clopidogrel use, in patients with diabetes remain unknown.

We performed an observational study exploring the relationship between stent type and clopidogrel use with long-term death and nonfatal myocardial infarction (MI) in a diabetic population undergoing PCI for de novo lesions.

Methods

Study population. The study cohort consisted of consecutive diabetic patients who underwent initial PCI at the Regional Cardiac Catheterization Laboratory located at the Kaiser Permanente Los Angeles Medical Center from October 1, 2002, to December 31, 2004. Diabetes mellitus was defined as any of the following: use of oral hypoglycemic agents or insulin, fasting plasma glucose values >126 mg/dl, or a random plasma glucose concentration ≥200 mg/dl. Measuring a repeat fasting or random plasma glucose on a subsequent day confirmed the diagnosis of diabetes. Kaiser Permanente is an integrated pre-paid health plan providing comprehensive care to more than 3 million members in Southern California. The health plan owns and operates medical centers, ambulatory care facilities, pharmacies, and laboratories.

All patients in this cohort underwent first time PCI and received either a BMS or DES. Exclusion criteria included: prior CABG, patient receiving both a BMS and DES during the index procedure, moderate to severe valvular disease, and nonhealth plan member because follow-up data were not available. Kaiser Permanente Southern California Institutional Review Board approval was received with waiver of the requirement for written informed consent.

Data collection. BASELINE DEMOGRAPHIC DATA. Baseline demographic data were obtained for review from the patients' medical record and health plan databases. For each patient, data on the distribution of coronary disease, blood pressure, body mass index, stent size, diameter, site of stent deployment, other medical history, and procedural data were obtained from health plan databases. Laboratory data that included serum creatinine, fasting low-density lipoprotein, and hemoglobin A1c were obtained at the time of cardiac catheterization or the most recent value before the procedure.

MEDICATION USE. Medication use was obtained by review of prescription records through an electronic pharmacy prescription database. The number of prescriptions filled, the daily dose, and the number of pills dispensed for each prescription beginning on the day of discharge after index PCI were used to calculate the duration of clopidogrel use. All patients received 75 mg daily of clopidogrel. Adjunctive pharmacotherapy with beta-blockers, statins, angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin II receptor blockers (ARBs) were also determined by electronic pharmacy prescription records. Use of these adjunctive medications was defined as 1 or more prescriptions for each drug after the PCI date. Aspirin use was not available through the electronic prescription database. However, all patients are instructed to take aspirin 325 mg daily for 30 days and then 81 mg daily indefinitely regardless of stent type.

Abbreviations and Acronyms

ACEI = angiotensin-converting enzyme inhibitor
ARB = angiotensin II receptor blocker
BMS = bare-metal stent(s)
CABG = coronary artery bypass grafting
DES = drug-eluting stent(s)
PCI = percutaneous coronary intervention

STUDY END POINTS. The primary end point of the study was a composite of all-cause death and nonfatal MI. Vital status was obtained from the medical record, health plan databases, and MORTLINK, which is a death database of the residents of California maintained by the state. Follow-up MI data were obtained by chart review and diagnosed by the patient's physician. We also used International Classification of Disease-9th Revision-Clinical Modification (ICD-9-CM) codes for MI to identify additional possible events in health plan databases. Any additional cases identified were then reviewed for confirmation. If troponin I was elevated in the appropriate clinical context (e.g., angina, anginal equivalent, or electrocardiogram with consistent abnormalities), then MI was confirmed. Periprocedural MI was defined as a creatine kinase-myocardial band (CK-MB) elevation >3 times the upper limit of normal.

Group assignments. The cohort was divided into DES and BMS groups, depending on the type of stent received. Each patient might have received more than 1 stent of the same class (DES or BMS). For this study both paclitaxel- and sirolimus-eluting stents were considered together in the DES group. The groups were then further divided on the basis of the duration of clopidogrel use. Clopidogrel users were those with continued use for >180 days from the index PCI date, whereas nonusers were those who stopped clopidogrel by 180 days.

Left-censored survival analysis was used to determine whether there were differences in the primary outcome between the DES and BMS groups stratified by clopidogrel use after the 6-month landmark. All patients who suffered death, MI, or underwent repeat revascularization (CABG or PCI) within 6 months of the index PCI were excluded. The remaining patients were categorized into 4 groups by stent type and clopidogrel duration: DES with clopidogrel, DES without clopidogrel, BMS with clopidogrel, and BMS without clopidogrel.

Statistical analysis. Continuous variables were reported as means ± SD or median and interquartile range if the distribution was not normally distributed. Normality was tested by the Shapiro-Wilk test. The analysis of variance test was used for normally distributed variables. The serum creatinine and cumulative stent length were non-normally distributed and compared with the Kruskal-Wallis test. Categorical variables are reported as percentage and abso-

lute values with comparisons made with the chi-square test or Fisher exact test where appropriate.

The Kaplan-Meier method was used to construct survival curves for the primary end point of death or nonfatal MI and censored for loss of health plan membership. Comparison between groups was made with the log-rank test. The left-censored survival analysis was from 6 months (180 days) to 18 months (545 days) after PCI. Cox-regression analysis for the primary end point was also performed. Variables with a p value ≤0.1 were entered into the multivariate model, yielding hazard ratios (HRs) and 95% confidence intervals (CIs). All tests are 2-tailed, with differences reported as significant if $p < 0.05$. All analyses were performed with SAS statistical software (version 9.1, SAS Institute, Cary, North Carolina).

Results

Study population. A total of 749 consecutive patients met all study criteria at the time of PCI. Of these, 41 died, suffered nonfatal MI, or underwent revascularization, and for 37 patients clopidogrel data were not available, leaving 671 in the 6-month left-censored survival analysis. All population characteristics (Table 1) are reported for the left-censored analysis cohort. There were 919 stents implanted in the study cohort. The mean age was 62.7 ± 10.8 years. The DES with clopidogrel group was slightly younger, 61.5 ± 10.2 ($p = 0.02$). The indication for the procedure, insulin use and hemoglobin A1c, a measure of glycemic control, were similar among all groups. Low-density lipoprotein levels and adjunctive medical therapy (e.g., statins, beta-blockers, ACEI/ARB) were higher among clopidogrel users in both the DES and BMS groups compared with clopidogrel nonusers. All groups were similar in the distribution of coronary vessels stented and number of significantly diseased arteries (>70% stenosis of a major epicardial coronary artery). However, cumulative stent length was greater in the DES groups. In the BMS groups, 97% of the stents were placed by April 2004, which is when the TAXUS DES (Boston Scientific, Natick, Massachusetts) received Food and Drug Administration (FDA) approval.

Clopidogrel compliance. Of the 749 patients, 37 (5%) were excluded because there was no available data on clopidogrel use in the health plan pharmacy records. The mean duration of clopidogrel use was 9.7 months. Duration of use was slightly greater among the DES groups (10.1 months) compared with the BMS groups (9.0 months), $p = 0.03$.

Survival analysis. The Kaplan-Meier analysis for the full cohort ($n = 749$) is shown in Figure 1. In the first 180 days after PCI, the cumulative incidence of death and nonfatal MI was similar between the BMS and DES groups. However, after 180 days the event rate was lower in the DES group ($p = 0.05$). A similar but nonsignificant trend was observed for mortality between the 2 stent types ($p = 0.33$).

In the left-censored analysis, freedom from death and nonfatal MI was determined for all 4 groups (Fig. 2). For DES ($n = 450$) compared with BMS ($n = 221$) the cumulative incidence of death or nonfatal MI was 3.1% versus 6.2% ($p = 0.08$), respectively. When stratified by clopidogrel status, the incidence in the BMS group was greatest among clopidogrel nonusers (12.2%) compared with users (3.5%), $p = 0.01$. Among the DES group, the cumulative incidence was 5.5% for clopidogrel nonusers compared with 2.2% for users, $p = 0.07$. Among clopidogrel nonusers, the incidence was 5.5% in the DES group and 12.2% in the BMS group, $p = 0.11$.

Freedom from death was also determined for all 4 groups (Fig. 3). For the DES group the incidence of death was 1.8% compared with 3.6% for the BMS group ($p = 0.18$). Among the BMS group, clopidogrel user versus nonuser incidence of death was 2.0% versus 6.8% ($p = 0.07$). Among the DES group, clopidogrel user versus nonuser incidence of death was 1.0% versus 3.9% ($p = 0.03$). The incidence of death in clopidogrel nonusers was 3.9% in the DES group and 6.8% in the BMS group ($p = 0.41$).

Clopidogrel duration and outcomes. The cumulative incidence of death or nonfatal MI was also assessed by clopidogrel duration. The full study cohort was divided into 3 groups by duration of clopidogrel use: <6 months, 6 to 9 months, and >9 months. The event rate for death or MI was 3.2% in the >9-month group, 9.4% in the 6- to 9-month group, and 16.5% in the <6-month group ($p < 0.001$) (Fig. 4). For death alone, the event rate was 0.5% in the >9-month group, 4.3% in the 6- to 9-month group, and 10.0% in the <6-month group ($p < 0.001$).

Among the patients who suffered death or MI during the left-censored analysis period, 82% were no longer clopidogrel users at the time of the event. The mean ± SD in days between clopidogrel cessation and death or MI was 188 ± 127 days and not significantly different between stent groups ($p = 0.12$).

Multivariate analysis. In the Cox regression analysis we calculated both the unadjusted and adjusted HRs for death and nonfatal MI. As previously described, the adjusted models included variables that were different among the 4 groups at a p value ≤0.1. This included adjunctive medical therapy with statins, beta-blockers, ACEI, ARB, number of stents deployed, stent diameter, and cumulative stent length. In the unadjusted model, taking BMS clopidogrel nonusers as a referent, the HRs and 95% CIs for DES with clopidogrel, DES without clopidogrel, and BMS with clopidogrel were HR 0.18 (95% CI 0.07 to 0.49, $p < 0.001$), HR 0.47 (95% CI 0.17 to 1.25, $p = 0.13$), and HR 0.26 (95% CI 0.09 to 0.78, $p = 0.02$), respectively. In the adjusted model, taking BMS clopidogrel nonusers as referent, the values for DES with clopidogrel, DES without clopidogrel, and BMS with clopidogrel were HR 0.22 (95% CI 0.08 to 0.62, $p = 0.005$), HR 0.39 (95% CI 0.13 to 1.13, $p = 0.08$), and HR 0.25 (95% CI 0.08 to 0.81, $p = 0.02$), respectively.

Table 1 Population Characteristics

	DES With Clopidogrel (n = 323)	DES Without Clopidogrel (n = 127)	BMS With Clopidogrel (n = 147)	BMS Without Clopidogrel (n = 74)	p Value
Age, yrs	61.5 ± 10.2	63.3 ± 12.1	64.3 ± 10.2	64.0 ± 11.6	0.02
Female, % (n)	30.1 (100)	33.9 (43)	29.9 (44)	36.5 (27)	0.72
Indication, % (n)					0.32
Stable angina	19.5 (63)	19.1 (24)	18.5 (27)	18.9 (14)	
Unstable angina	36.8 (119)	46.8 (59)	48.0 (70)	37.8 (28)	
NSTEMI	29.4 (95)	27.0 (34)	23.3 (34)	28.4 (21)	
STEMI	14.2 (46)	7.1 (9)	10.3 (15)	14.9 (11)	
Prior MI, % (n)	55.7 (180)	58.3 (74)	55.1 (81)	64.9 (48)	0.50
Insulin, % (n)	20.7 (67)	31.5 (40)	20.4 (30)	27.0 (20)	0.07
HgA1c, % (n)	7.4 ± 1.7	7.3 ± 1.6	7.6 ± 1.8	7.6 ± 1.9	0.40
LDL (mg/dl)	114 ± 37	103 ± 36	121 ± 39	111 ± 41	0.001
Creatinine (mg/dl)	1.0 (0.8–1.1)	1.0 (0.9–1.2)	1.0 (0.8–1.1)	1.0 (0.8–1.2)	0.36
Hemoglobin (mg/dl)	13.5 ± 1.7	13.3 ± 2.0	13.3 ± 1.7	13.0 ± 1.7	0.09
Ejection fraction (%)	0.61 ± 0.15	0.62 ± 0.15	0.63 ± 0.15	0.59 ± 0.16	0.55
Body mass index (kg/m^2)	30.7 ± 6.2	30.1 ± 5.8	30.0 ± 5.9	29.4 ± 5.9	0.23
AoSBP, mm Hg	144 ± 31	148 ± 28	146 ± 33	142 ± 32	0.36
AoDBP, mm Hg	71 ± 12	72 ± 11	71 ± 14	67 ± 12	0.03
Clopidogrel duration, % (n)					
>6 months	71.8 (323)	0	66.5 (147)	0	0.16
>9 months	55.3 (249)	0	48.9 (108)	0	0.12
Other medications, % (n)					
Statins	96.6 (312)	89.8 (114)	95.9 (141)	82.4 (61)	<0.0001
Beta-blockers	93.5 (302)	86.6 (110)	92.5 (136)	87.8 (65)	0.08
ACEI or ARB	93.2 (301)	83.5 (106)	92.5 (136)	83.8 (62)	0.003
Angiographic variables					
No. of stents	1.4 ± 0.6	1.3 ± 0.7	1.4 ± 0.6	1.5 ± 0.7	0.03
Mean stent diameter (mm)	2.9 ± 0.3	3.0 ± 0.3	3.2 ± 0.5	3.0 ± 0.5	<0.0001
Cumulative stent length (mm)	23 (18–33)	20 (16–31)	16 (13–26)	18 (15–26)	<0.0001
No. of diseased vessels					0.65
1-vessel disease	58.8 (190)	63.0 (80)	58.5 (86)	59.5 (44)	
2-vessel disease	32.8 (106)	29.9 (38)	28.6 (42)	32.4 (24)	
≥3-vessel disease	8.4 (27)	7.1 (9)	12.9 (19)	8.1 (6)	
Stent location, % (n)					
LAD	50.5 (163)	44.9 (57)	42.2 (62)	41.9 (31)	0.27
Diagonal*	4.0 (13)	1.6 (2)	2.7 (4)	0 (0)	0.25
Circumflex	16.4 (53)	19.7 (25)	20.4 (30)	18.9 (14)	0.71
Obtuse marginal	9.9 (32)	8.7 (11)	10.2 (15)	12.2 (9)	0.89
RCA	28.8 (93)	30.7 (39)	35.4 (52)	31.1 (23)	0.56
PDA or PLV*	3.1 (10)	3.9 (5)	2.7 (4)	8.1 (6)	0.23
Ramus intermediate*	0.9 (3)	2.4 (3)	0 (0)	1.4 (1)	0.20
Stent use by year					
2002	0	0	51.0 (30)	49.0 (29)	
2003	36.9 (113)	15.4 (47)	35.0 (107)	12.8 (39)	
2004	68.9 (210)	26.2 (80)	3.0 (9)	2.0 (6)	

Data are reported as mean ± SD, median (range), or % (n). *Comparison made with Fisher exact test.

ACEI = angiotensin-converting enzyme inhibitor; AoDBP = aortic diastolic blood pressure; AoSBP = aortic systolic blood pressure; ARB = angiotensin II receptor blocker; BMS = bare-metal stent(s); DES = drug-eluting stent(s); HgA1c = hemoglobin A1c; LAD = left anterior descending; LDL = low-density lipoprotein; MI = myocardial infarction; NSTEMI = non–ST-segment elevation myocardial infarction; PDA = posterior descending artery; PLV = posterior lateral branch; RCA = right coronary artery; STEMI = ST-segment elevation myocardial infarction.

We also performed pairwise multivariate adjusted analysis for the DES and BMS groups for clopidogrel user versus nonuser. In the unadjusted model, the HR and 95% CI for clopidogrel user versus nonuser in the DES group was HR 0.39 (95% CI 0.14 to 1.11, p = 0.08) and in the BMS group was HR 0.27 (95% CI 0.09 to 0.79, p = 0.02). In the multivariate adjusted analysis these were HR 0.48 (95% CI 0.16 to 1.47, p = 0.48) and HR 0.21 (95% CI 0.06 to 0.73, p = 0.01) for the DES and BMS groups, respectively.

Discussion

In this observational study the extended use of clopidogrel, defined as >6 months from the index PCI, was associated

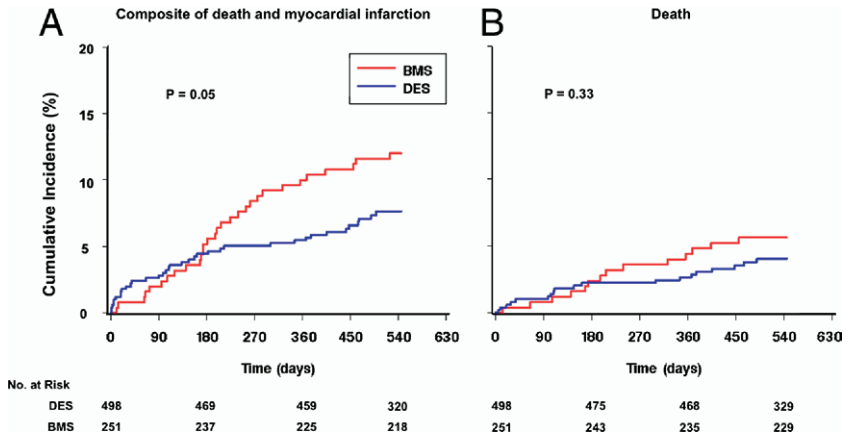

Figure 1 **Outcomes by Stent Type**

Cumulative incidence of death and nonfatal myocardial infarction or death only by stent type for the full cohort (n = 749). BMS = bare-metal stent(s); DES = drug-eluting stent(s).

with significantly greater freedom from death and MI in the BMS group (p = 0.01) and from death in the DES group (p = 0.03). Among clopidogrel nonusers, a group at high risk for late stent thrombosis, the event rate for death and MI was similar in the DES and BMS groups (p = 0.11). Mortality was also similar in the DES without clopidogrel group compared with the BMS without clopidogrel group (p = 0.40). These observations suggest that the extended use of clopidogrel is associated with a reduction in death or death and nonfatal MI. This observed benefit likely results

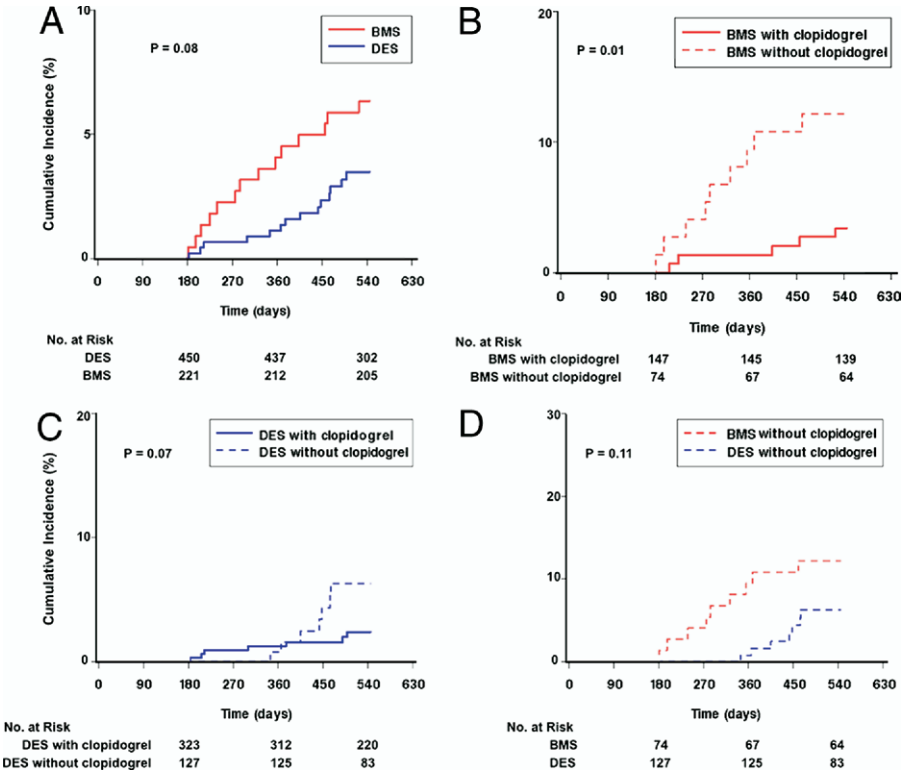

Figure 2 **Left-Censored Survival Analysis for Death and Nonfatal Myocardial Infarction**

Cumulative rates of death and nonfatal myocardial infarction by stent type and clopidogrel use in the left-censored survival analysis. Abbreviations as in Figure 1.

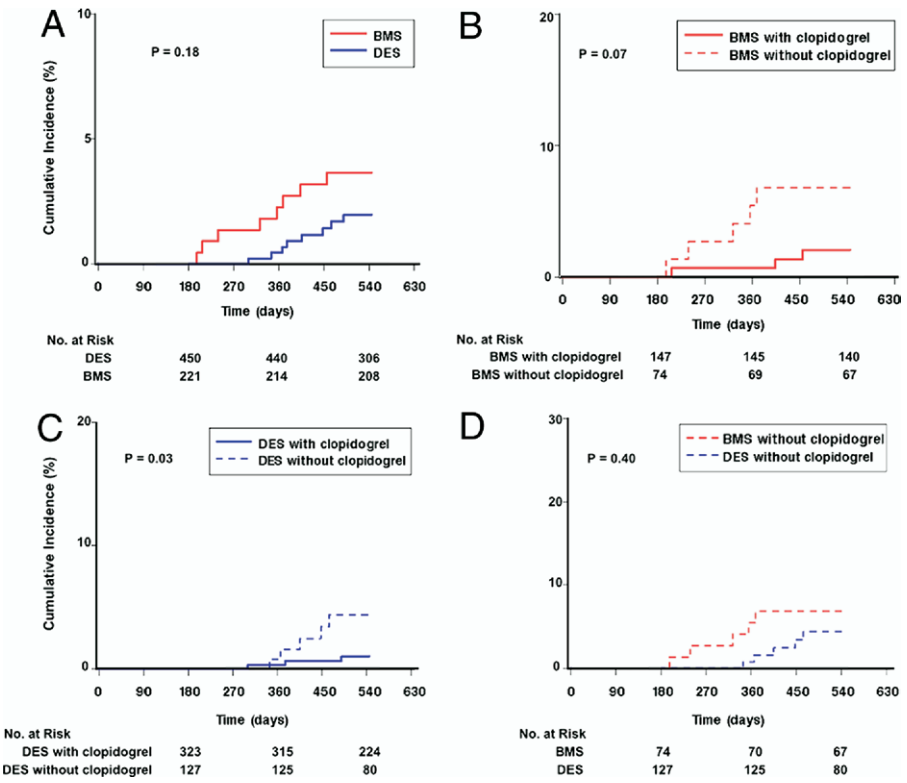

Figure 3 **Left-Censored Survival Analysis for Death**

Cumulative rates of death by stent type and clopidogrel use in the left-censored survival analysis. Abbreviations as in Figure 1.

from the dual action of clopidogrel—the prevention of stent thrombosis but also clinical events at other sites in the coronary tree.

In contrast to our observations, 2 prior 6-month left-censored survival analyses show increased death and nonfatal MI with DES compared with BMS among clopidogrel nonusers (14,15). However, this study relates specifically to patients with diabetes, whereas in the prior studies the majority of the patients (70% to 80%) were not diabetic. The biologic response to DES might be altered in the diabetic compared with the nondiabetic patient, which might explain, in part, the difference between studies. For example, an in vitro study shows that rapamycin does not seem to impair smooth muscle migration to the same degree in a hyperglycemic environment compared with an euglycemic environment (16), which might account for the greater late loss observed in diabetic patients. This might lead to higher rates of endothelialization and thus lower rates of late stent thrombosis in diabetic patients. This might also explain, in part, the higher rates of target lesion revascularization observed in diabetic patients in clinical trials. It remains unclear the extent to which other potential mechanisms such as hypersensitivity or inflammatory reactions to the stent polymer, tissue factor expression leading to a prothrombotic environment, late stent malapposition due to thrombus resolution, or stent strut fracture occur in diabetic patients and result in adverse events (17–20).

Clopidogrel use. There are no clinical trial data that address the required duration of clopidogrel use after DES placement. The FDA approved DES with 3 to 6 months of clopidogrel therapy, the protocol-specified minimum duration in the CYPHER (Cordis Corporation, Miami Lakes, Florida) and TAXUS stent pivotal trials, respectively (5,6). Recent data suggest that longer duration of clopidogrel use might be necessary given the slight increase in stent thrombosis observed with DES. However, prolonged use needs to be balanced against the bleeding risk (21) and cost associated with clopidogrel therapy. In this study, the incidence of death and MI by clopidogrel duration was determined. In both the full cohort and the left-censored analysis cohort the extended use of clopidogrel was associated with a decrease in death and the composite of death and nonfatal MI ($p < 0.01$). These results complement those of the CREDO (Clopidogrel for the Reduction of Events During Observation) trial (22), and PCI CURE (PCI in the Clopidogrel in Unstable Angina to Prevent Recurrent Ischemic Events) trial (23).

Patients in this study were insured health plan members. This might have altered the risk factor mix for death and

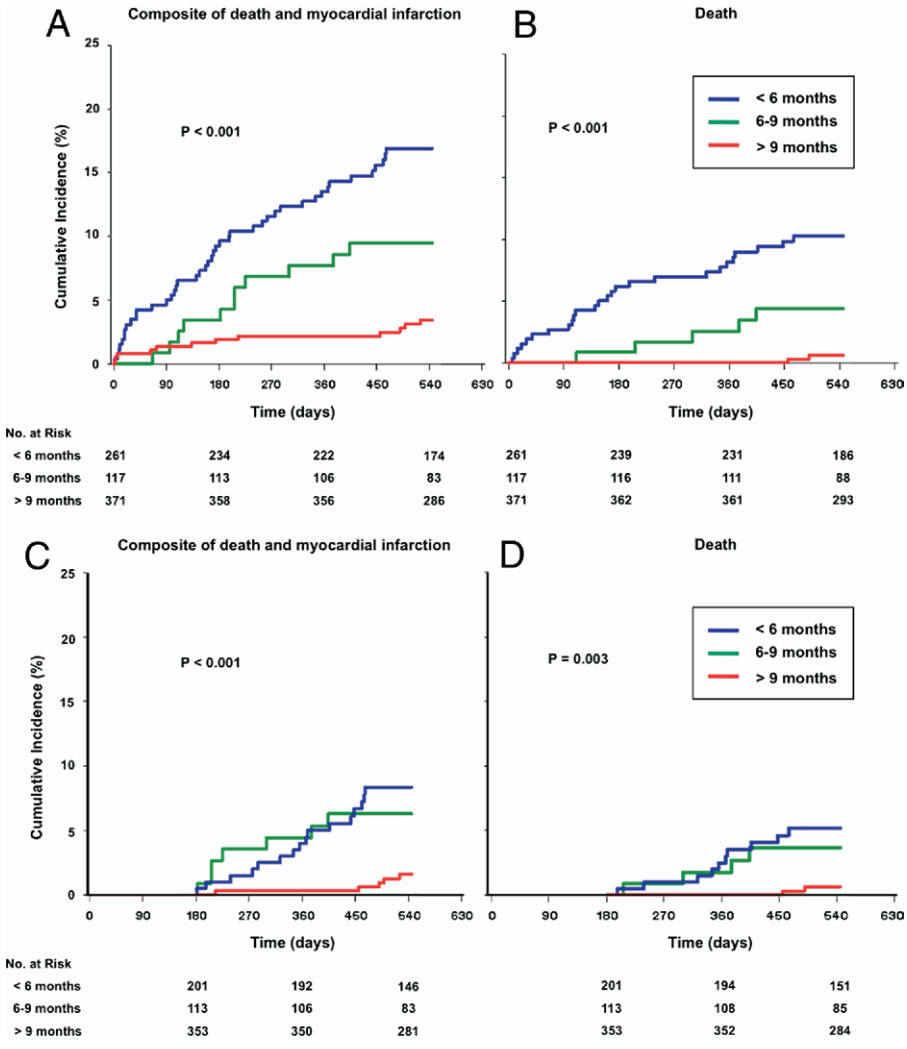

Figure 4 Outcomes by Clopidogrel Duration

(A and B) Cumulative incidence of death and nonfatal myocardial infarction or death only by clopidogrel duration for the full cohort (n = 749). **(C and D)** Cumulative incidence of death and nonfatal myocardial infarction or death only by clopidogrel duration in the left-censored analysis.

nonfatal MI and long-term prognosis. Compliance with clopidogrel as measured by prescriptions filled was 95 percent. This is in contrast to the observation in the PREMIER (Prospective Registry Evaluating Myocardial Infarction: Events and Recovery) registry that almost 1 in 7 patients were no longer taking a thienopyridine by 30 days (24). This is important, because premature discontinuation of clopidogrel has been identified as the most powerful predictor of stent thrombosis (13). The compliance in our population might have even been greater than reported, because internal health plan data show that up to 5% of the health plan members receive medications at nonhealth plan pharmacies. However, we were not able to account for this in our estimates. All patients before discharge receive a written list of medications and a follow-up appointment with a cardiologist in 1 to 4 weeks, which might also contribute to the overall compliance with medical therapy and improved outcomes with DES use.

Study limitations. This was an observational analysis, and clopidogrel use was not randomly assigned. The decision to continue beyond the FDA label specifications might be correlated with unidentified prognostic factors or institutional biases. After the introduction of the TAXUS DES in the U.S. we routinely recommended a minimum of 6 months of clopidogrel to all patients regardless of DES type. Second, we assumed persons refilling prescriptions were continuously taking clopidogrel. The largest quantity dispensed was 90 tablets, requiring patients to return to the pharmacy for additional medication. However, we did not perform pill counts, which could more accurately reflect medication use. Nevertheless, using prescription records has been shown to be more accurate than patient self-reporting

of medication use, because self-reporting is limited by recall and other biases (25,26). Third, aspirin use was not available through the pharmacy prescription database, and our inability to adjust for aspirin noncompliance remains a limitation. However, given that clopidogrel was typically used on average for several months, it is likely that patients were also compliant with aspirin therapy. All patients receive the same instructions for aspirin use as previously stated. Lastly, left-censored analysis can create a potential bias due to the possible differential truncation of patients before the censoring point. In contrast, the cumulative incidence analyses do not suffer from such bias and yield cumulative incidence of death or death and MI from the index PCI date.

Conclusions

Patients with diabetes require a multifaceted approach with risk factor modification and contemporary medical and interventional therapy to target both progression of coronary disease and the culprit lesion. Our data suggest that with contemporary medical therapy the extended use of clopidogrel was associated with fewer adverse events in the BMS and DES groups. Among clopidogrel nonusers, a group at high risk for stent thrombosis, the event rates for death and MI were similar in the DES and BMS groups. However, definite conclusions on the safety and efficacy of DES and the appropriate duration of clopidogrel use in a diabetic population can only be drawn from prospective randomized trials.

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